

## **REMARKS**

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

As indicated in the Office Action Summary, claims 1-26 are pending. Claims 1, 12 and 14 are amended herein to remove specific terms. The abstract is amended herein to remove the phrase "said". Thus, no new matter is presented by way of the present Amendment. Applicants reserve the right to file a continuation or divisional application directed to any subject matter canceled by way of the present Amendment.

Applicants note with appreciation that claims of Groups I-III have been rejoined for examination.

### ***Specification***

The abstract is objected to for the recitation of "said". The abstract is amended herein to address this issue.

### ***Rejections Under 35 U.S.C. § 112, First Paragraph***

Claims 1-26 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for protein kinase C inhibitor or alpha-antitrypsin, purportedly does not provide enablement for any inhibitor. Applicants respectfully traverse.

In paragraph 3, on page 2 of the Office Action, the Office Action states that the inhibitor of interest is a protein kinase C inhibitor. For purposes of clarification, Applicants submit this is incorrect. Rather, the present invention is directed to a protein C inhibitor.

Regarding the assertion of lack of enablement for the use of any inhibitor with the present invention, Applicants submit that enablement is present in the specification combined with the skill in the art. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to breadth of the claims, nature of the invention, state of the prior art, level of one of ordinary skill, level of predictability in the art, amount of direction provided by the inventor, the existence of working examples; and quantity of experimentation needed to make or use the invention based on the content of the disclosure.

*In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

To this end, Applicants enclose herewith four references disclosing a monoclonal antibody against antitrombin. Antitrombin is another serine proteinase inhibitor, which is similar to protein C inhibitor. This evidence supports the argument that the present invention may be used with inhibitors of this kind.

In combination with the specification, Applicants submit that the claims are enabled.

***Rejections Under 35 U.S.C. § 112, Second Paragraph***

Claims 1-26 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite.

Claims 1 and 22 stand rejected for the recitation of "a cleaved and uncomplexed form of said inhibitor" as it is purportedly unclear what constitutes "substantially no specific affinity for said inhibitor." Applicants submit that this term would be clear to the skilled artisan, for the following reasons.

Upon the formation of a complex between a serine proteinase, such as activated protein C, and a serine proteinaase inhibitor, such as the protein C inhibitor, a small but variable proportion of the inhibitor is cleaved in the reactive site loop without complex formation. This results in a cleaved inhibitor and a free, active serine proteinase.

This cleaved form of the inhibitor also has the reactive site loop inserted in  $\beta$ -sheet A, just as a complexed inhibitor (see Strandberg, K. et al. (2000) *Biochemistry* 39:15713-15720). The term cleaved inhibitor is very clear, and described in Strandberg, K. et al. and by P.W. Gettins in *Chemical Reviews* (2002 102:4751-483). By way of explanation, the antibody had no affinity for the uncleaved, uncomplexed form of the inhibitor, *i.e.*, the dominant of the inhibitor in blood plasma. This conclusion is based on the finding that no affinity can be demonstrated between the two with surface plasmon resonance. Moreover, affinity chromatography using gel with immobilized antibody did not bind or even retard the uncleaved form of the

inhibitor indicating no affinity for this form of the inhibitor (see Figure 1 of the present application). Finally, Figure 3 of the application shows that standard curves in plasma and buffer were identical within experimental error despite the about 105-fold higher concentration of native inhibitor than of complexed inhibitor. Thus, Applicants submit that it would be clear to the skill artisan as to what is claimed in claims 1 and 22.

Claim 1 stands rejected for the recitation of "derivative thereof" as it is purportedly unclear what is "derivative" in the context, *e.g.*, chemical modification, or recombinant substitution. Applicants submit that the term derivative is well known in the art, and would be well understood by the skilled artisan. In support, Applicants submit the definition of "derivative" from the *Oxford Dictionary of Biochemistry and Molecular Biology*, Smith Ed., (1997) p. 165. Based on the specification and what is known in the art, Applicants submit the meaning of "derivative" as used in claim 1 would be clear to the skilled artisan.

Claim 12 stands rejected for the recitation of "a suitable enzyme" as it is purportedly not clear what constitutes "suitable" in this context. Claim 12 is amended herein to remove the term "suitable". Thus, this rejection is obviated.

Claim 14 stands rejected for the recitation of "a similar lanthanide" as it is purportedly unclear what is the "similar lanthanide." Claim 14 is amended herein to remove the term "similar lanthanide". Thus, this rejection is obviated.

### CONCLUSION

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, a Notice of Allowance is respectfully requested.

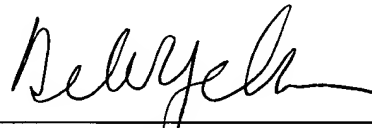
In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (703) 836-6620 so that prosecution of the application may be expedited.

Respectfully submitted,

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By:



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